VALUE IN HEALTH REGIONAL ISSUES 3C (2014) 1–4

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/vhri

Revisit What Is Next for Pharmacoeconomics and Outcomes Research in Asia

Hong Li, PhD, MPH[1,2,3,*], *Surachat Ngorsuraches, PhD*[4]

[1]*Bristol Myers Squibb Company, Wallingford, CT, USA;* [2]*Cincinnati University, Cincinnati, OH, USA;* [3]*Jiao-Tong University, Shanghai, China;* [4]*Faculty of Pharmaceutical Sciences, Prince of Songkla University, Songkhla, Thailand*

ABSTRACT

As part of the global trend to address the constrained resources for population health care coverage, the concepts of pharmacoeconomics (PE) and health technology assessment (HTA) have been introduced to Asia in the last decade. Medicines are just one of numerous types of innovative technologies developed to address unmet medical need. Many of these medicines receive a great deal of attention because of their potential impact on limited health care budgets. There are a few key challenges for using PE and HTA in making informed decisions regarding the value of a given new health care technology in an Asian country. These challenges include 1) recognizing the multidimensional aspects of PE and HTA, which can include both health care and political considerations; 2) involving stakeholders (with a focus on patients) in decision making; 3) balancing short- and long-term overall benefits of innovative medicines; and 4) giving consideration to specific local cultural and health care characteristics.

Keywords: Asia, health care, HTA, innovative technologies, patients, pharmaceuticals, pharmacoeconomics, population.

Introduction

In 2004, Doherty et al. [1] evaluated the early evolution of pharmacoeconomics (PE) in Asia, including China, Japan, South Korea, Hong Kong, Taiwan, and Singapore. On the basis of their assessments, the authors proposed that controlling health care expenditure and increasing the efficient use of limited health care resources were the two most important reasons for applying PE to health care in Asia. The authors predicted that the need for PE in Asian health care would result in more academic studies and consequently increased numbers of publications on this subject, which would enhance appreciation for the use of PE in Asia. In these authors' view, this trend would be so even in the absence of formal processes for evaluating PE in these countries.

Over the last 8 years since the Doherty et al. article was published, there has been a rapid advancement in the understanding and implementation of PE in Asia. This is evidenced by many published research articles on the topic. In addition, there have been many important events related to PE development in the region, including the establishment of National Evidence-based Healthcare Collaborating Agency [2,3], which acts as one of the resources providing information on health economics to support decision making on pharmaceutical reimbursement by Health Insurance Review Agency in South Korea [4]. In Taiwan, a health technology assessment (HTA) group has been established within the Center of Drug Evaluations to evaluate pharmaceutical pricing and reimbursement submission and HTA has been included as part of the National Act of 2nd Generation of Healthcare Insurance Reform [5]. In China, PE guidelines have been published [6] and there is ongoing active academic research on HTA [7]. In addition, a group of scholars from mainland China, Taiwan, and Hong Kong created the Greater China (Huaxia) Forum on Health Economics. In Japan, there is a plan to conduct a pilot HTA program by the Ministry of Health, Labor and Welfare [8]. The creation of International Society of Pharmacoeconomics and Outcomes Research Asia Consortium has greatly fostered the development of PE in the region. After 8 years since the landmark article by Doherty et al., PE activities and research are found in more Asian countries than the originally mentioned in their article, such as Thailand, Malaysia, India, Indonesia, and the Philippines [9].

The economy in Asia and the global advancement of innovative medicines have played an important role in pushing the PE development in the region. In the last two decades, there has been greater economic growth in Asia than in other parts of the world. In 2011, health care expenditure as a percentage of gross domestic product (GDP) was quite high across all Asian countries, with Japan and South Korea having the highest proportion of GDP

Derived from a presentation made at the 3rd plenary session, ISPOR 5th Asia Pacific Conference, September 4, 2012, Taipei: "Recognizing Value Is Key for Adopting Innovative Technologies in Healthcare Coverage in Asia."

* Address correspondence to: Hong Li, Global Health Economics & Outcomes Research, Bristol Myers Squibb Company, 5 Research Parkway Way, Wallingford, CT 06492, USA.

E-mail: hong.li@bms.com.

2212-1099/$36.00 – see front matter Copyright © 2014, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

http://dx.doi.org/10.1016/j.vhri.2013.04.001

(9.6% and 6.9%, respectively) [10]. Health care costs represent a significant proportion of the GDP, indicating the significant efforts being made by the public sector to provide health care coverage to citizens in these countries. This effort also likely reflects increased demands on health care due to aging populations, evolution of disease patterns, and access to improved health technologies. One particular pressure on health care costs is the increased number of potential medicines being developed worldwide. For example, a global statistics showed that by 2011, the number of new medicines under clinical development ranged from 96 for antiviral treatments (hepatitis B virus [HBV], hepatitis C virus [HCV] and HIV) to 1527 for various tumors [11]. Although not every candidate was or will be successfully developed, a good number are anticipated to eventually reach Asian markets. Approvals of these new medicines certainly put pressure on limited health care resources in these Asian countries.

To revisit the question of "what is next for pharmacoeconomics in Asia" that Doherty et al. asked 8 years ago, this article discusses key challenges in adopting innovative technologies, including 1) multidimensional feature of applying PE, 2) stakeholders' involvement, 3) patients' role, 4) focus on overall benefit, and 5) local adaptation of PE. Among all the challenges, the critical point will be how the core value of these innovative medicines should be evaluated in different Asian health care systems.

While Research on PE Is Technical, Application of the PE Assessment Tools Takes Place in a Multidimensional Plane, Including Public Policy and Political

Bootman et al. [12] defined PE as "description and analysis of the costs of drugs to the health care system and the society". O'Donnell et al. [13] defined HTA as "a form of policy research that examines short and long-term consequences of the application of a health-care technology". The Health Technology Assessment International Association definition for HTA is "the systematic evaluation of properties, effects or other impacts of health care interventions" [14]. Based on these varied definitions, HTA can be viewed as broadly related to health care in general and can involve strategies and more aspects; PE is applied health economics in the narrower area in pharmaceuticals. Regardless of the definitions, the successful use of PE or HTA requires a high degree of subject-specific knowledge. Discussions among PE experts, however, can become so technical that they may not consider other important dimensions of PE such as the implication of PE on public policy decisions. Therefore, for reason of simplicity, "PE" is used because this article mainly focuses on medicines.

When talking about PE for pharmaceuticals, in economics theory, we are talking about opportunity costs, always making trade-offs between different options. For example, allocating a resource to one disease area makes it unavailable for use in other disease areas. Similarly, if a resource is used for the health care sector, it cannot be used for education or housing. In daily life, policymakers always make these trade-offs by prioritizing the use of limited resources. Providing resources to care for one or two individuals is typically a technical decision; however, deciding the use of limited public resources to care for the health of a country's populations is certainly a political decision that is likely highly politically charged.

In addition, setting up a proper legal framework to provide legal positions for the application of PE is important, and can also be quite political. Recent examples from Europe are the process by which requirements of cost-effectiveness analysis were incorporated into the Social Security Law in France, and similarly in Spain, the Royal Decree Law addressed the issue of cost-effectiveness analysis (CEA) for reimbursing new medications [15,16]. Another example with a long history in the legal framework is found in Australia where Pharmaceutical Benefits Advisory Committees were set up in 1950 s [17]. This is important for at least two reasons: first, ensuring transparency in the PE process for all stakeholders; second, denying access to innovative technologies, especially those developed in other countries, could have an impact on trade treaties between countries. Therefore, the use of PE to assist decisions on drug reimbursement can go beyond the health care sector. Unless one has the legal framework moving in the right direction, one cannot properly implement PE evaluations in technical areas, such as setting up guidelines or criteria in conducting PE assessments.

Involvement in Decision Making Should Be Inclusive for All Stakeholders

Because the use of PE is very complex, assessment of innovative technologies by these approaches certainly should involve not only experts on PE and policymakers but also other stakeholders. These stakeholders would comprise health care providers, patients and patient groups, and the pharmaceutical industry. Involvement of these stakeholders provides different perspectives that will contribute to the overall evolution of PE evaluations. Currently, Taiwan and South Korea are actively engaging experts in PE and clinicians (physicians and pharmacists) together with government decision makers in their PE assessments. Later, other stakeholders, such as patient groups, become involved in this process. However, both these countries are lagging in their active integration of pharmaceutical industry representatives (the source of the clinical trial and PE data) into the process.

Two important considerations should be kept in mind in regard to stakeholder involvement. The first is that having a dialogue does not mean that there has to be agreement at all times and active discussion is a key part of the process of implementing PE. The second is the importance of early engagement of all stakeholders, something that is necessary for sufficient consultation prior to making final decisions. In the political world, especially with Asian cultures, it is important to keep in mind that once a decision is made, it may take a very long time to amend that decision. Active and early engagement, therefore, is key to the successful use of PE evaluations in decision making.

Keeping Patients in Mind Is Critical for Adopting Innovative Technologies

The use of PE normally involves technical experts because it is a complex, multidisciplinary science. Keeping the patient in mind, however, is important for any decision making that involves PE evaluations. A policy decision is always made at the population level; therefore, when PE assessments are conducted, every analysis could impact a patient's life. In other words, we are not only talking about numbers but also giving information that will support a decision that would significantly impact patients in our care.

It is well known that in medical practice the flow of information is usually asymmetrical between clinicians and patients. The hallmark of a traditional medical practice model is that clinicians make most of the decisions for patients. In part, to overcome this one-sided flow of information, in 2009, US Congress authorized the creation of an institute called the Patient-Centered Outcomes Research Institute, which is a non-physician source of information for patients [18]. The goal of this institute is to provide the best available evidence so that patients can make informed decisions. Active patient engagement is even regarded as the "blockbuster drug of the century,"

which represents a significant trend toward a new standard of care in the near future [19].

Getting patients involved in clinical decision making is more than just having them sign an informed consent form; before clinical decisions are made, physicians should describe the full picture of the disease and its treatments to patients, including the risks and benefits. In the example of Beth Israel Deaconess Medical Center in the United States, patients have open access to their records (i.e., the "OpenNotes" Approach). In Asia, patient participation in medical decision making is in its infancy and the patients' voice is relatively weak. This is probably due to Asian cultures in which patients usually have little influence on medical decisions, either at the individual level or at the population level. This situation, however, is changing in part because of information exchanges via the Internet. Patient groups are emerging in Taiwan and South Korea [20], and organizations for patient care are also developing in mainland China. Similar to other parts of the world, patients in Asia are playing an increasingly important role in making decisions regarding their health care. Therefore, when talking about developing PE to assist decision making of health care policy in Asia, we should keep in mind this important recent evolution in Asian medical practice.

Although the number of patient groups has grown, obtaining their perspectives to help inform PE decision making remains challenging in Asia as well as worldwide. Therefore, setting up the proper infrastructure and to keep communication flowing between patient groups and policy decision making is critical. One practical way to accomplish this is to have patient representatives on committees that would provide advice to an HTA body, such as the formal consultation to the consumer community in the United Kingdom and Australia [21].

Two more items are worth mentioning. First, PE decisions may impact not only patients but also their caregivers; this would be particularly true for cancer patients and/or elderly patients with chronic diseases. A recent report on caregivers shows that this group tends to also experience caregiver burden and related medical issues such as depression, which generate physician visits and hospitalizations. This is probably due to, at least for some cases, the fact that these caregivers have to deal with depressing situations with their family members or significant others [22]. Second, PE evaluations should not be conducted at the expense of delaying innovative technologies and medicines for patients. For example, under the current pricing evaluation system in Japan, the listing of a price for a newly approved medicine is normally provided within 2 to 3 months. Whether this time frame could still be maintained in Japan after an HTA process is implemented seems challenging.

Focusing on Overall Health Care Benefits Rather Than Drug Costs Only

When discussing PE assessment for new innovative pharmaceutical products, we are discussing the overall value of those medicines; the focus is not on the price of the medicines except in the case of pure cost minimization analysis, where the health outcomes associated with the new medicine are similar as those with the comparator medicine. For example, there are 12 million patients with various tumors living in the United States. In 2011, the American Society of Clinical Oncology identified 12 oncology treatments that have the potential to reduce cancer mortality, of which 10 involved new medicines. As another example, the annual rate of death from HIV/AIDS was reported as 16.2% before highly active antiretroviral theraphy (HAART) therapy was introduced in 1996. In 2010, the HIV/AIDS-related mortality rate had been reduced to 2.7% [21]. Similarly, studies in Asia found not only reductions in HBV-related complications due to better control by new medications but also lower health care costs [23–25]. These are good examples of how innovative medicines can benefit patients, the health care system, and society, both clinically and economically.

As mentioned earlier, an HTA system can have various formats with or without formal assessment requirements on CEA. In a number of HTA systems, both CEA and budget impact analysis (BIA) would be required by an authority when a product's manufacturer applies for pricing and/or reimbursement status. While a cost-effectiveness model would take into consideration all costs (depending on the perspective) and clinical efficacy (or effectiveness), a BIA, most of the time, would assess only pharmacy costs. Even though a BIA is built for the purpose of understanding the financial impact of an additional innovative medicine on a formulary for reimbursement, using BIA to evaluate pharmacy costs may be less helpful to comprehensively oversee and manage health care costs. Therefore, the pros and cons of using both CEA and BIA should be carefully examined and balanced when making health care policy.

The Need to Consider Local Country-Specific Characteristics When Using PE to Evaluate New Medical Technologies

The creation of *Value in Health Regional Issues* is a good indicator of the increasing number of publications on PE in Asia. Because the concepts and principles of PE were created originally in the Western world, the concept should be tailored to the socioeconomic situations, health care systems, medical practices, cultures, and value systems of different Asian countries.

Adoption of PE assessments into population health care coverage decisions requires the followings: adequate understanding of the technical areas and sufficient number of qualified researchers or scholars to perform the analysis. A typical example to illustrate the first point is the application of quality-adjusted life-years (QALYs) when used as a measure of effectiveness across therapeutic areas or conditions in a CEA. While it is not that difficult to apply the principle of CEA, it is quite challenging to decide how to apply the concept of the QALY in Asia. Health economists in the United Kingdom and Australia, who are culturally similar, may argue that the QALY is a straightforward numeric and objective measure to apply; however, properly generating this number in Asia is challenging because this is affected by local culture and value systems. The value of a QALY as derived from the Western world is always perceived as too high for developing countries, including those in Asia. As an alternative to the commonly cited value for QALY used in the United States or the United Kingdom, a two-time multiple of the country's annual GDP was proposed by the World Health Organization [26]. Even if this alternative was applied in Asia, it would still be tough to use a single value for all diseases or conditions, and for an entire population. The recent discussion in the National Institute for Health and Clinical Excellence around an alternative cancer-specific QALY for oncology patients could serve as a good example of how challenging this can be even in countries such as the United Kingdom in which QALY analysis is well established [26]. Asia is no exception to this situation. Therefore, while mathematical analysis may be feasible, criteria for evaluating certain PE-related outcomes need to be made on the basis of local situations.

Because research on PE in Asia is still in its early stage of development relative to the Western world [27], use of results from studies outside that did not include Asian countries may need to be viewed with caution because they may not be applicable or generalizable to at least some (if not all) of the countries. A medication that may reduce the length of hospital stays in the United States would show potential cost saving in

that country, especially for complicated cases in which hospitalization can be expensive. For example, annual costs of hospitalizations for preterm or low-birth-weight babies can be as high as $5.1 billion in the United States [28]. Yet, because of differences in the health care cost structure in Asian countries compared with the United States, results from US analysis may not be applicable to Asian health care systems and caution is required when US data are referenced in Asia.

Proper use of PE also requires qualified researchers or scholars who are good in both technical know-how and understanding of local cultures and health care systems. Both the consideration of country-specific characteristics and the availability of knowledgeable PE researches are equally important for the successful incorporation of innovative technologies into population health coverage in Asia.

Conclusions

Incorporating innovative technologies, in medicines in this case, into health care coverage in Asia is a double-edge sword: on the one hand, Asian countries can learn a lot from the experiences of the Western world, which may shorten the learning curve; on the other hand, the experiences and findings from the Western world may not be directly applicable to Asian countries; therefore, the applications need to be tailored to specific local cultures and health care systems. Based on the development in the last one decade, it is clear that the concepts of PE have been extensively introduced to facilitate decision making for health care resources in Asia. This is also recognition of the core value of innovative technologies that are relevant to Asian patients and health systems, which will be the key for future developments.

On the basis of the discussions above, authors of this article predict that PE research as a whole would become more extensive. Collaboration on PE academic research will be further developed at the regional level. How to apply PE methodology developed in the Western world will continue being the theme in research in Asia. HTA agencies would set up their evaluation criteria, including a process, on a model based on experiences from various countries. Different from the academic research, government agencies in Asia may be more in favor of practical solutions to policy issues, such as how to handle budget impacts in the short term. Although value still needs to be further defined in an empirical sense by various Asian countries, a value-based price for pharmaceuticals will become a hot topic. This may be a good opportunity to have a win-win dialogue between the decision makers and the pharmaceutical industry. As the overall economy continues to grow, patient-reported outcomes, including quality of life, will receive more attention during the policy-making process. Eventually, proper applications of PE, especially when research is transferred into health care policy, can be made only at the country level.

Acknowledgments

The authors are indebted to David Grainger and Jim Patrick Doherty for their valuable comments on this manuscript. In addition, the authors are grateful to the constructive editing by Betsy Goodwin.

Source of financial support: No funding is provided to this manuscript.

REFERENCES

[1] Doherty J, Kamae I, Lee KC, et al. What is next for pharmacoeconomics and outcomes research in Asia? Value Health 2004;7:118–32.
[2] Park SH, Lee SM. Evidence-based decision-making and health technology assessment in South Korea. Value Health 2008;11(Suppl. 1):S163–4.
[3] Lee SII, Park MH, Lee EK, Ahn JH. How to harmonize HTA and value for innovation? Issue Panels: Session I. ISPOR 5th Asia Pacific Conference. Taipei, September 2–4, 2012.
[4] Yang BM, Bae EY, Kim JH. Economic evaluation and pharmaceutical reimbursement reform in South Korea's National Health Insurance. Health Aff 2008;27:179–87.
[5] Lang HC. Drug policy update and trend in Taiwan. Beijing: Huaxia Forum, May 5, 2012.
[6] China guidelines for pharmacoeconomic evaluations China J Pharm Econ 2010;3:5–43.
[7] Chen YY, Banta D, Tang ZL. Health technology assessment development in China. Int J Technol Assess Health Care 2009;25(Suppl. 1):202–9.
[8] PhRMA and EFPIA. HTA in Japan. Document on file. 2012.
[9] ISPOR Asia Consortium. Available from: http://www.ispor.org/consortiums/asia.asp. [Accessed October 19, 2012].
[10] World Bank Indicator. Available from: http://data.worldbank.org/indicator/SH.XPD.PUBL/countries. [Accessed August 10, 2012].
[11] PhRMA. New drug approvals in 2011: 2012 report. Available from: http://www.pharma.org/research/publications. [Accessed August 16, 2012].
[12] Bootman JL, Townsend RJ, McGhan WF. Principles of Pharmacoeconomics. Harvey Whitney Books, 2005.
[13] O'Donnell J, Pham SV, Pashos CL, et al. Health technology assessment: lessons learned from around the world—an overview. Value Health 2009;12(Suppl. 2):S1–5.
[14] HTAi/INAHTA. Resources for health technology assessment. Available from: http://www.htai.org/. [Accessed October 19, 2012].
[15] LFSS 2012. Available from: http://www.securite-sociale.fr/IMG/pdf/lfss_2012_en_chiffres-3.pdf. [Accessed October 25, 2012].
[16] Royal Decree Law 16/2012, Spain. Available from: http://www.garrigues.com/es/Publicaciones/Boletines/Documents/Updates-Farma-May-2012.pdf. [Accessed October 25, 2012].
[17] Low J, et al. Australia Pharmacey Law & Practice. National Library of Australia, 2010.
[18] PCORI. Available from: http://www.pcori.org/about/. [Accessed August 12, 2012].
[19] Patient engagement is the blockbuster drug of the century (part 2). Available from: http://www.forbes.com/sites/davechase/2012/10/13/patient-engagement-is-the-blockbuster-drug-of-the-century-part-2/. [Accessed October 18, 2012].
[20] ISPOR 5th Asia Pacific Conference. Taipei, September 2–4, 2012. Available from: http://www.ispor.org/conferences/Taipei0912/program_090312.asp#plenarysession. [Accessed October 18, 2012].
[21] PhRMA 2012 profile pharmaceutical industry. Available from: http://www.phrma.org/research/publications. [Accessed August 12, 2012].
[22] Mori A, Goren A, Gilloteau I, et al. Quantifying the burden of caregiving for patients with cancer in Europe. ESMO 2012.
[23] Chen CJ, Yang HI, Su J, et al. Risk of hepatocellular carcinoma across a biological gradient of serum hepatitis B virus DNA level. JAMA 2006;295:65–73.
[24] Hosaka T, Suzuki F, Kobayashi M, et al. Long-term entecavir treatment reduces hepatocellular carcinoma incidence in patients with chronic hepatitis B. Poster 1419064. Boston, USA: The 63rd AASLD, November 9–13, 2012.
[25] Wu B, Li T, Chen HF, et al. Cost effectiveness of nucleoside analog therapy for hepatitis B in China, a Markov analysis. Value Health 2010;13:592–600.
[26] World Health Organization. Macroeconomics and Health: Investing in Health for Economic Development: Report of the Commission on Macroeconomics and Health. Geneva, Switzerland: World Health Organization, 2001.
[27] Drummond M. Key principles for the conduct of HTA for resource allocation decisions. Available from: http://www.pp.u-tokyo.ac.jp/HTA/events/2012-09-06/documents/hta20120906-drummond.pdf. [Accessed October 12, 2012].
[28] Russell RB, Green NS, Steiner CA, et al. Cost of hospitalization for preterm and low birth weight infants in the United States. Pediatrics 2007;120:1–9.